Department of Health and Human Services
Maine People Living Safe, Healthy and Productive Lives

Paul R. LePage, Governor Mary C. Mayhew, Commissioner

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July 8, 2016

Dawson P. Julia
241 Depot Street
Unity, ME 04988

RE: Public Petition to add Addiction to Opiates and drugs derived from chemical synthesis to the List of Debilitating Medical Conditions

Dear Mr. Julia:

This letter will serve as the Department's final written decision regarding your Petition dated January 8, 2016, to add "Addiction to Opiates and drugs derived from chemical synthesis" to the list of debilitating medical conditions. This petition request was received by the Department on January 12, 2016. For the reasons set forth in the attached Briefing Memoranda, which is incorporated by reference, I hereby declare that the Petition is denied. It should be clearly understood that this decision was reached after careful consideration of the Petition and information provided by the Petitioner; other medical research, written and oral testimony submitted at the public hearing held on April 19, 2016, and consultation with two (2) licensed Maine physicians. The decision was made in accordance with 22 M.R.S. §§ 2422(2)(D) and 2424(2), and 10-CMR Ch. 122 §§ 3.2 through 3.6.

This decision constitutes final agency action, which is subject to judicial review pursuant to Rule 80C of the Maine Rules of Civil Procedure and 5 M.R.S. § 11001 et seq., Maine Administrative Procedures Act.

Sincerely,

Mary C. Mayhew
Commissioner

MCM/klv

cc: Sheryl Peavey, Chief Operating Officer, Maine CDC, DHHS
Christopher Pezzullo, State Health Officer, Maine CDC, DHHS
James Markiewicz, Director, Division of Public Health, Maine CDC, DHHS
Marietta D'Agostino, Program Manager, MMMP, Maine CDC, DHHS

Department of Health and Human Services
Maine People Living Safe, Healthy and Productive Lives
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Public Petition
Maine Medical Use of Marijuana Program

PETITIONS MUST BE FILED WITH THE DIVISION OF LICENSING AND REGULATORY SERVICES ATTENTION - MMMP

Adding debilitating medical conditions. In accordance with 22 M.R.S. §2422 (2) (D), the Department has adopted rules regarding the consideration of petitions to add medical conditions or diseases to the existing list of debilitating medical conditions. Pursuant to 10-144 CMR, Ch. 122, the Department shall provide an opportunity for a public hearing to comment on petitions. After a hearing, the Commissioner shall approve or deny a petition within 180 days of its submission.

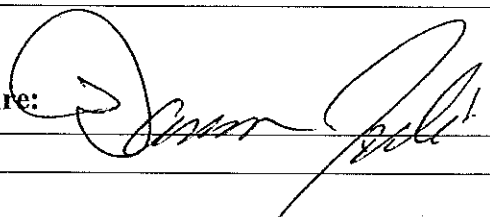
Public petitions adding debilitating medical conditions must comply with 10-144 CMR, Ch. 122, Sec. 3.2 *et. al.*, including the following:

- The petition must clearly identify the specific debilitating disease or medical condition.
- The petition must include reputable scientific evidence that supports the use of marijuana for the treatment of the disease or medical condition.
- The petition must include sufficient evidence to demonstrate that the medical use of marijuana would benefit qualifying patients with the disease or medical condition.
- The petition must include evidence that marijuana therapy is sufficiently effective to warrant its use.

Section 1. Petitioner Information

Name (first, middle initial, last)
Dawson P Julia

Mailing Address (where mail is received)	**Telephone:**
241 Depot Street **Unity, ME 04988** (city, state, zip code)	(207) **649** - **0005** **Email address:** **dawsonpjulia@gmail.com**

Signature:  **Date:** **1/8/2016**

Section 2. Debilitating Disease or Medical Condition (one form per disease or condition)

Name of Debilitating Disease or Medical Condition:
Addiction to Opiates and drugs derived from chemical synthesis.

Section 3. Reputable Scientific Evidence – Please provide a list of citations to reputable scientific evidence and attach copies of referenced materials to this petition. If additional space is needed, please attach another Page 2 of this petition.

- Please see the many studies that have been attached to this form
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FOR OFFICE USE ONLY

Date Petition Received: 1/12/16

Date Decision Due (180 days from date received): 9/10/16

Petition Approved: _____

Petition Denied: ✓

(See attached written Decision)

Commissioner Signature: _____

Maine Center for Disease Control and Prevention
An Office of the Department of Health and Human Services
Paul R. LePage, Governor Mary C. Mayhew, Commissioner

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TO: Mary C. Mayhew, Commissioner

FROM: Christopher Pezzullo, DO, State Health Officer

Siiri Bennett, MD, State Epidemiologist

SUBJECT: Medical Marijuana Advisory Committee Report on the Petition for the *Use of Medical Marijuana for the Treatment of Addiction to Opiates and Drugs Derived from Chemical Synthesis*

CC: Sheryl Peavey, Chief Operating Officer, Maine Center for Disease Control

DATE: July 1, 2016

Background

Maine DHHS is responsible for ensuring that there is reputable scientific evidence that supports the medical use of marijuana for qualifying patients with one of the approved diseases or conditions listed in Section 3.1 of the Rule. As stated in 3.2.4, the petitioner must include sufficient evidence to demonstrate that the medical use of marijuana would benefit qualifying patients with the disease or medical condition.

Marijuana contains over 100 cannabinoids, which are the active chemical components of cannabis. Delta-9-tetrahydrocannabinol (THC) is considered the most psychoactive component of marijuana. However, the scientific literature around the use of medical marijuana often refers to Cannabidiol (CBD), another component of marijuana, which shows a number of pharmacological effects with therapeutic potential. CBD is considered safer and more uniform in its composition than whole marijuana; it is associated with less variability in response to therapy given and is of greater clinical value. Other than the potential issues of immunosuppression and sedation at very high doses, there do not appear to be any other safety issues associated with CBD. Several of the studies reviewed below reference the use of CBD.

Process

In reviewing public petitions to add to the list of debilitating medical conditions set forth in Section 3.1 of the Rule, the Committee looks for similar reputable scientific evidence such as those that guide the process and requirements set forth by the Food and Drug Administration (FDA) for the approval of new drugs. Specifically, the Committee evaluates whether the studies submitted by the petitioner show that the drug is safe and effective for its proposed use based on the following:

- Results of preclinical animal testing that show that ***the drug is effective in animals for the treatment or management of the medical condition proposed***
- Results of Clinical Trials (Phase 1) in human volunteers that ***document the most frequent side effects and drug metabolism and secretion***
- Results of Clinical Trials (Phase 2) in humans that ***demonstrate the effectiveness of the drug in people with the disease or condition proposed***
- Results of Clinical Trials (Phase 3) in humans that ***investigate dosages and use of the drug in combination with other drugs in different populations***

The Committee analyzes study results, looks for weaknesses in study design or analyses, and looks for gaps in data around safety and efficacy. The Committee determines if it agrees with the petitioner's results and conclusions or

whether additional information is needed before the proposed disease or condition can be added to the approved list of debilitating conditions.

Mr. Dawson Julia submitted the aforementioned petition on January 8, 2016. Members of the Committee reviewed the testimony presented on April 19, 2016 and reviewed the dozens of documents submitted by the petitioner and persons who gave written or oral testimony or both. The Committee reviewed additional published literature on marijuana and cannabinoid substances. For the purposes of this review, the Committee defined 'drugs derived from chemical synthesis' as synthetic opiate-like substances.

The Medical Marijuana Advisory Committee (Drs. Christopher Pezzullo and Siiri Bennett) met on May 26, 2016 to review the application for the Use of Medical Marijuana for the Treatment of Addiction to Opiates and Drugs Derived from Chemical Synthesis.

Findings

The Committee received the following documents for review:

- 2 systematic reviews
- 5 peer-reviewed publications of scientific studies in humans
- 1 human case report
- 3 survey studies in humans
- 9 published scientific studies in non-humans (primarily mice and rats)
- 5 other articles
- 9 abstracts
- 17 media releases, media articles, reviews of papers, information pages from the internet
- 19 emails or letters sharing personal experiences
- 136 MMMP Patient Impact Survey responses
- 5 charts, graphs or tables

Additional studies identified by the Committee were also reviewed.

The following short list highlights the most meaningful findings:

1. A 2014 Media Advisory from the JAMA Network entitled "Lower Opioid overdose death rates associated with state medical marijuana laws" lists overdose death rates in states with and without medical marijuana laws; however, ***no causal relationship is shown.***
2. A study in rats published in Addiction Biology (2013) by Katsidoni et al concludes that cannabidiol interferes with brain reward mechanisms responsible for the rewarding effects of opioids. While encouraging, ***further research and replication of results needs to be done in humans.***
3. Another promising study in rats by Yamaguchi et al in Brain Research (2001) looks at the effects of endogenous cannabinoid on naloxone-precipitated withdrawal in morphine-dependent mice. It ***suggests that cannabinoids may inactivate withdrawal syndromes***. However, this has never had human replication.
4. One study referenced (Navarro et al. Functional interaction between opioid and cannabinoid receptors in drug self-administration from the Journal of Neuroscience [2001]) suggests an interaction between opioid and cannabinoid systems in behavior related to addiction and suggests new strategies for treatment of opioid dependence in rats. ***It does not fully quantify the interaction, noting only that some types of interactions occur between endogenous opioid and cannabinoid systems.***
5. One randomized trial is being conducted by Yasmin Hurd who is looking at "acute and short-term effects of cannabidiol administration on cue-induced craving in drug-abstinent heroin dependent subjects" in humans. The trial is currently in progress and if positive, will need to be replicated.

6. There has been one other randomized trial by Raby et al in American Journal of Addiction (2009) on "Intermittent marijuana use is associated with improved retention in naltrexone treatment for opiate-dependence". Researchers found that intermittent use rather than no use or consistent use of marijuana might improve adherence to naltrexone treatment—***suggesting that too much or too little marijuana could have deleterious effects***. However it does not suggest that marijuana use would replace naltrexone treatment.
7. In a paper by Prud'homme, Cata and Justras-Aswad in Substance Abuse: Research and Treatment (2015), the authors performed a systematic review of the evidence for Cannabidiol as an intervention for addictive behavior. ***No human study was found showing the impact of Cannabidiol on opioid-addictive behaviors.***
8. One review paper by Scavone, Sterline and Van Bockstaele in Neuroscience (2013) on "Cannabinoid and opioid interactions: implications for opiate dependence and withdrawal" reviewed the evidence from animal and clinical studies that look at the interactions between endocannabinoids and opiates. The studies reviewed suggest that ***cannabinoids may be useful in managing opiate dependence and withdrawal and the authors note that such studies may support novel interventions in management of opiate dependence and withdrawal.***
9. In further research, Committee members identified *one article that contradicted the studies put forward in the testimonies. An article by Fattore et al in Neuropharmacology (2005) on "Cannabinoid CB(1) antagonist SR 141716A attenuates reinstatement of heroin self-administration in heroin-abstinent rats" found that* ***heroin and cannabinoid agonists both reinstated heroin-seeking behavior in rats.***

Conclusions

While the animal and case studies and individual testimonies presented are compelling and point towards possible future approaches to the treatment of opioid addiction, ***studies in humans that support marijuana use for the treatment of opioid addiction have not yet been published***. There are a number of promising animal studies that suggest interactions between cannabinoids and opiate receptors and support the need for further research in this area. Human trials are now underway.

No information was presented and no information could be found on appropriate marijuana potency, content and dosage when used for the treatment of opiate addiction.

No data on the safety of using marijuana for treatment of opioid addiction were submitted with the petition, nor were *protocols* for effective use of medical marijuana in opioid and opiate addiction offered.

Given the lack of rigorous human studies on the use of marijuana for the treatment of opioid addiction (only one clinical trial has been completed) and the lack of any safety or efficacy data, the Committee cannot conclude that the use of Medical Marijuana for treatment of opioid addiction is safe.

Recommendations

There are no published scientific data on the efficacy of Medical Marijuana in the treatment of human opioid addiction. No safety data were presented. **The Committee, therefore, recommends against adding opioid addiction to the list of approved conditions for Medical Marijuana**.

However, it is noteworthy that many with opioid/opiate substance use disorder began using these substances due to a perceived need to treat chronic pain. Many of the reviewed studies suggested that medical marijuana could have an opiate-sparing effect in the treatment of chronic pain. While this was not discussed by the petitioner, chronic pain is already an approved diagnosis for treatment with medical marijuana in Maine.